

REMARKS

By the present amendment claims 1, 4, 5 and 13-16 have been amended; claims 2, 6 and 25 have been canceled without prejudice or disclaimer; and no claims have been added. Subsequent to the entry of the present amendment, claims 1, 3-5, 9-24 and 26-27 are pending and at issue. The amendments and additions add no new matter as the claim language is fully supported by the specification and original claims.

Claim Objections

Claim 25 stands objected to as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim. Without acquiescing to the rationale presented in the Office Action, Applicants have canceled claim 25 rendering the objection moot.

Rejections under 35 U.S.C. §112, Second Paragraph

Claims 4, 5 and 13-16 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully traverse the rejection as it applies to the pending claims.

With regard to claims 4 and 5, the Office Action alleges that there exists insufficient antecedent basis for the limitation “said linker molecule”. Without acquiescing to the rationale presented in the Office Action, Applicants have amended claims 4 and 5 to depend from claim 3 which recites “a linker molecule” thereby providing antecedent basis. Accordingly, Applicants respectfully request withdrawal of the rejection.

With regard to claims 13-16, the Office Action alleges that there exists insufficient antecedent basis for the limitation “strand”. Without acquiescing to the rationale presented in the Office Action, Applicants have amended claims 13-16 to recite “region” which has antecedent basis in claim 1. Accordingly, Applicants respectfully request withdrawal of the rejection.

With regard to claims 15 and 16, the Office Action alleges that the claims are indefinite for reciting “antisense and/or sense” and then further limiting only the antisense strand. Without

In re Application of:
Axelsson and Good
Application No.: 10/582,946
Filed: March 2, 2007
Page 7

PATENT
Atty Docket No.: INDEX1140-1

acquiescing to the rationale presented in the Office Action, Applicants have amended claims 15 and 16 such that both the antisense and sense region is further limited. Accordingly, Applicants respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C. §102

Claims 1-4, 9-14, 21, 22, and 25-27 stand rejected under 35 U.S.C. §102(e) as allegedly anticipated by Khvorova et al. (2007/0031844). Applicants respectfully traverse the rejection as it applies to the pending claims. Applicants have canceled claims 2 and 25 rendering the rejection moot as to such claims.

In part, the Office Action alleges Khvorova et al. discloses a sequence that is complementary to 18 of 21 nucleotides of SEQ ID NO: 5 and which is 17 of 21 nucleotides of SEQ ID NO: 9 and is therefore substantially homologous to the siRNA comprised of SEQ ID NO: 5 and SEQ ID NO: 9.

To anticipate, a single reference must inherently or expressly teach each and every element of claimed invention. *In re Spada*, 15 USPQ2d 1655 (Fed Cir. 1990); and *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). MPEP § 2131. Without acquiescing to the rationale presented in the Office Action, and in order to expedite prosecution of the instant application, Applicants have amended the claims to recite the exact sequences of SEQ ID NO: 5 and SEQ ID NO: 9 in addition to incorporating the limitation of claim 6 (the sense region of the siRNA molecule consisting of SEQ ID NO: 9) into claim 1. Applicants submit that Khvorova et al. fails to disclose the exact sequences as recited in the amended claims.

Accordingly, Applicants respectfully submit that Khvorova et al. fails to meet each and every element of the claimed invention and therefore does not meet the standard under 35 U.S.C. §102(e). For these reasons, Applicants request that the rejection be withdrawn.

Rejections under 35 U.S.C. §103

Claims 1-4, 6, 9-14 and 21-27 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over Khvorova et al. (2007/0031844). Additionally, claims 1-6 and 9-27 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over Khvorova et al. (2007/0031844), as applied to claims 1-4, 6, 9-14 and 21-27, and further in view of Fosnaugh et al. (2003/014732). Applicants respectfully traverse the rejections as it applies to the pending claims. Applicants have canceled claims 2, 6 and 25 rendering the rejection moot as to such claims.

In part, the Office Action alleges that it would have been obvious in view of Khvorova et al. to make an siRNA molecule comprising SEQ ID NO: 5 and SEQ ID NO: 9 because the reference allegedly teaches siRNAs with a range of complementarity as well as a sequence which is only one-nucleotide difference from SEQ ID NO: 9.

The recent U.S. Supreme Court decision in the *KSR International v. Teleflex Inc.* (82 USPQ 2d 1385), modified the standard for establishing a *prima facie* case of obviousness. Under the *KSR* rule, three basic criteria are considered. First, some suggestion or motivation to modify a reference or to combine the teachings of multiple references still has to be shown. Second, the combination has to suggest a reasonable expectation of success. Third, the prior art reference or combination has to teach or suggest all of the recited claim limitations. Factors such as the general state of the art and common sense may be considered when determining the feasibility of modifying and/or combining references.

Applicants respectfully submit that the Office Action fails to establish a *prima facie* case of obviousness in light of the amended claims based on the teachings of Khvorova et al. and/or Fosnaugh et al. The human NF-kappa-B transcription factor p65 DNA binding subunit is about 1760 bp in length. Thus, identifying the exact target regions within this sequence is not trivial and there would be an undue burden for the skilled person to find target regions giving optimal RNA interference. Figure 1 in the present application shows that different siRNA compounds give different results. For example, SEQ ID NO: 8 and 12 confer much less RNA interference than either SEQ ID NO: 5 and 9 and SEQ ID NO: 6 and 10. Further, while the Fosnaugh et al.

In re Application of:
Axelsson and Good
Application No.: 10/582,946
Filed: March 2, 2007
Page 9

PATENT
Atty Docket No.: INDEX1140-1

reference gives no guidance of how to find the optimal target region of the p65 subunit of the NF-kappa-B gene, the optimal target sequences disclosed in the Khvorova et al. reference for the p65 subunit of the NF-kappa-B gene (also known as RelA) are very different than that of the present invention as evidenced by siRNA duplex pools disclosed for RelA (see, Khvorova et al., Table X, page 86, 2nd column, RelA).

Accordingly, Applicants respectfully submit the Office Action fails to establish a *prima facie* case of obviousness in light of the amended claims based on the teachings of Khvorova et al. and/or Fosnaugh et al. and therefore does not meet the standard under 35 U.S.C. §103(a). For these reasons, Applicants request that the rejection be withdrawn.

In re Application of:
Axelsson and Good
Application No.: 10/582,946
Filed: March 2, 2007
Page 10

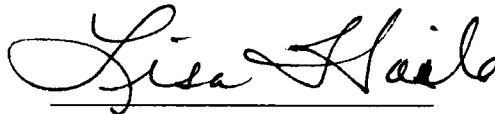
PATENT
Atty Docket No.: INDEX1140-1

Conclusion

In view of the amendments and above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

No fee is deemed necessary with the filing of this paper. However if any fees are due, the Commissioner is hereby authorized to charge any fees, or make any credits, to Deposit Account No. 07-1896 referencing the above-identified attorney docket number.

Respectfully submitted,



Lisa A. Haile, J.D., Ph.D.
Registration No. 38,347
Telephone: (858) 677-1456
Facsimile: (858) 677-1465

Date: February 12, 2008

DLA PIPER US LLP
4365 Executive Drive, Suite 1100
San Diego, CA 92121-2133
USPTO Customer No. 28213